REMARKS

At the outset, Applicants would like to thank Examiners Roark and Gambel for the courtesy of the telephonic Examiner's Interview conducted with Applicants' representatives on March 4, 2004, during which the outstanding rejections in the above-referenced application were discussed.

Applicants note that the amendment filed July 17, 2003 has been entered.

Applicants further note that the Examiner has amended the Attorney Docket Number from GIN-005 to 36119-126. However, Applicants would like to point out that the correct Attorney Docket Number for the instant application should read 36119-126**US1**. Applicants respectfully request that the Attorney Docket Number be corrected to 36119.126US1 in future correspondence.

Claims 1, 55, 60, 75 and 87-94 were pending in the instant application.

I. Withdrawal of Prior Rejections

Applicants gratefully acknowledge that the Examiner has accepted the Petition to Correct Inventorship under 37 C.F.R. § 1.48(a), filed on July 17, 2003, and has changed the inventorship of the application to include Bruce L. Levine, and accordingly, withdrawn three prior rejections (Office Action, page 2, section 4). Specifically, the Examiner has withdrawn a rejection under 35 U.S.C. § 102(f) of claims 1, 55, 87-90, 92 and 94 (Office Action, page 4, section 9), and the rejections under 35 U.S.C. § 102(a) and § 103(a) over Levine *et al.* (*Science* **272**:1939-1942, 1996) of claims 1, 55, 87-90, 92 and 94 (Office Action, page 4, section 10). Applicants also note that the Examiner has withdrawn the previous rejection of claims 1, 55, 60, 75, 91 and 93 under 35 U.S.C. § 103(a) as being unpatentable over Chang (U.S. Patent No. 6,129,916) in view

of the alleged art-recognized use of avidin-biotin complexes to couple antibodies to solid phase surfaces, as evidenced by Shattil (U.S. Patent No. 5,561,047) (Office Action, page 9, section 16).

II. Amendments to the Specification

The Examiner objected to the Amendment filed July 17, 2003, for allegedly introducing new matter. Specifically, the Examiner opined that the correction of the material on page 18, in the paragraph at lines 8-20, seventh line, is not obvious. Without acquiescing to the Examiner's objection and solely for the purpose of furthering prosecution of the instant application, Applicants have cancelled the correction herewith. Thus, Applicants aver that this objection under 35 U.S.C. § 132 has been overcome.

III. Amendments to the Claims

Claims 1, 55, 60, 75 and 92-94 have been cancelled without prejudice or disclaimer of the subject matter contained therein. Applicants reserve the right to pursue the subject matter of these claims in this or future related applications.

Claims 95-107 have been newly added. Support for the newly added claims can be found throughout the application as filed. Specifically, support can be found at page 2, line 25 to page 3, lines 1-11; page 7, lines 19-25; page 8, lines 11-14; page 13, lines 34-35; page 14, lines 12-13; page 16, lines 3-6; page 25, line 36 to page 26, lines 1-5; page 27, lines 1-2, and line 34 to page 28, lines 1-2; and Example 7, bridging pages 37 and 38. No new matter has been added as a result of these amendments to the claims.

Accordingly, claims 95-107 are currently pending in the instant application.

IV. Rejection under 35 U.S.C. § 112, first paragraph

Claims 1, 55, 60, 75, 87-88 and 91-94 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly not providing "enablement for the method comprising contacting the T cells with solid phase surfaces other than a bead" (Office Action, page 3, section 7, first paragraph).

Claims 1, 55, 60, 75, 87-88 and 91-94 have been cancelled. Thus, this rejection as it applies to these claims has been rendered moot. However, we address this rejection as it may apply to the new claims 95-107.

The currently pending claims recite "bead" and not "solid phase surface." Accordingly, with the entry of the new claims, Applicants aver that this rejection under 35 U.S.C. § 112, first paragraph, has been rendered moot.

V. Rejection under 35 U.S.C. § 102(e) over Chang

Claims 1, 55, 60, 75, 87-89, 92 and 94 remain rejected under 35 U.S.C. § 102(e) as purportedly being anticipated by Chang (U.S. Patent No. 6,129,916), as evidenced by Levine *et al.* (Office Action, page 4, section 12).

Specifically, the Examiner alleges that "Chang teaches and claims a method of increasing the activation or proliferation of T cells comprising contacting T cells with a microbead coupled with a plurality of binding molecules specific for an antigen on a human T cell. Chang teaches that an embodiment of the invention includes using microbeads that comprise a binding molecule that is an antibody to CD3 paired with another binding molecule that is specific for T cells, including an antibody to CD28" (Office Action, page 4, section 12, paragraph 3). The Examiner relies on Levine *et al.* for allegedly evidencing "that resistance of T cells to infection with the M-tropic (CCR5-

dependent) HIV-1 strain inherently occurs following contact with a solid phase surface comprising an anti-CD3 antibody and an anti-CD28 antibody *in vitro*." The Examiner further alleges that "downregulation of CCR5 also is inherent as evidenced by the resistance [of T cells] to infection by M-tropic HIV strains" (Office Action, page 5, section 12, paragraph 5).

Claims 1, 55, 60, 75, 87-88 and 91-94 have been cancelled. Thus, this rejection as it applies to these claims has been rendered moot. However, we address this rejection as it may apply to the new claims 95-107.

To anticipate a claim, a prior art reference must disclose ***each and every limitation*** of the claimed invention, either explicitly or inherently. *See In re Schreiber*, 128 F.3d 1473, 1477 (Fed. Cir. 1997). Absence of a claim element from a prior art reference negates anticipation. *Atlas Powder Co. v E. I. du Pont de Nemours & Co.*, 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984). Anticipation of a patent claim requires a finding that the claim at issue "reads on" a prior art reference. See *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 781, 227 USPQ (BNA) 773, 778 (Fed. Cir. 1985). In other words, if granting patent protection on the disputed claim would allow the patentee to exclude the public from practicing the prior art, then that claim is anticipated, regardless of whether it also covers subject matter not in the prior art. *See id.* at 781.

New claims 95 and 96, and claims depending thereon, recite an *ex vivo* method for downregulating HIV-1 fusion cofactor (or CCR5) expression in a T cell comprising contacting the T cell with a bead comprising an anti-CD28 antibody or a fragment thereof and an anti-CD3 antibody or a fragment thereof; and measuring the level of HIV-1 fusion cofactor (or CCR5) expression in said contacted T cell, wherein the level of HIV-1 fusion cofactor expression (or CCR5) in said contacted T cell is lower than the

level of the HIV-1 fusion cofactor (or CCR5) expression in a T cell not contacted with said bead.

New claims 97 and 98, and claims depending thereon, recite a method for downregulating HIV-1 fusion cofactor (or CCR5) expression in a T cell, comprising contacting the T cell *in vivo* with a bead comprising an anti-CD28 antibody or a fragment thereof and an anti-CD3 antibody or a fragment thereof; and measuring the level of HIV-1 fusion cofactor (or CCR5) expression in said contacted T cell, wherein the level of HIV-1 fusion cofactor (or CCR5) expression in said contacted T cell is lower than the level of the HIV-1 fusion cofactor (or CCR5) expression in a T cell not contacted with said bead.

Applicants respectfully submit that Chang fails to teach Applicants' claimed method. Chang does not teach measuring the level of HIV-1 fusion cofactor (or CCR5) expression in a T cell contacted with a bead comprising an anti-CD28 antibody or a fragment thereof and an anti-CD3 antibody or a fragment thereof, wherein the level of HIV-1 fusion cofactor (or CCR5) expression in said contacted T cell is lower than the level of the HIV-1 fusion cofactor (or CCR5) expression in a T cell not contacted with said bead, as required by Applicants' claimed method.

Because, Chang does not teach ***each and every element*** of Applicant's claimed method, Chang does not anticipate Applicants' claimed invention. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

VI. <u>Rejection under 35 U.S.C. § 102(b) over Levine *et al.*</u>

Claims 1, 55 and 87-90 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Levine *et al.* (*Int. Immunol.* 7:891-904, 1995), as evidenced by Levine *et al.* (*Science* **272**:1939-1942, 1996).

The Examiner alleges that Levine *et al.* (*Int. Immunol.*) teach a method comprising contacting T cells with a solid phase surface comprising an anti-CD3 antibody and an anti-CD28 antibody *in vitro*. The Examiner relies on Levine *et al.* (*Science*) as described *supra*.

Claims 1, 55, 60, 75, 87-88 and 91-94 have been cancelled. Thus, this rejection as it applies to these claims has been rendered moot. However, we address this rejection as it may apply to the new claims 95-107.

As discussed above, to anticipate a claim, a prior art reference must disclose ***each and every limitation*** of the claimed invention, either explicitly or inherently. *See In re Schreiber*, 128 F.3d 1473, 1477. Absence of a claim element from a prior art reference negates anticipation. *Atlas Powder Co. v E. I. du Pont de Nemours & Co.*, 750 F.2d 1569, 224 USPQ 409.

New claims 95 and 96, and claims depending thereon, recite an *ex vivo* method for downregulating HIV-1 fusion cofactor (or CCR5) expression in a T cell comprising contacting the T cell with a bead comprising an anti-CD28 antibody or a fragment thereof and an anti-CD3 antibody or a fragment thereof; and measuring the level of HIV-1 fusion cofactor (or CCR5) expression in said contacted T cell, wherein the level of HIV-1 fusion cofactor expression (or CCR5) in said contacted T cell is lower than the level of the HIV-1 fusion cofactor (or CCR5) expression in a T cell not contacted with said bead.

New claims 97 and 98, and claims depending thereon, recite a method for downregulating HIV-1 fusion cofactor (or CCR5) expression in a T cell, comprising contacting the T cell *in vivo* with a bead comprising an anti-CD28 antibody or a fragment thereof and an anti-CD3 antibody or a fragment thereof; and measuring the level of HIV-1 fusion cofactor (or CCR5) expression in said contacted T cell, wherein the level of HIV-1 fusion cofactor (or CCR5) expression in said contacted T cell is lower than the level of the HIV-1 fusion cofactor (or CCR5) expression in a T cell not contacted with said bead.

Levine *et al.* (*Int. Immunol.*) are directed to investigating apparent differences, if any, between the CD28 ligands, B7-1 and B7-2, in the ability to co-stimulate T cells of healthy donors (page 892, right column, "Cells and reagents"). Levine *et al.* do not in any way teach or suggest measuring the level of HIV-1 fusion cofactor (or CCR5) expression in a T cell contacted with a bead comprising an anti-CD28 antibody or a fragment thereof and an anti-CD3 antibody or a fragment thereof, wherein the level of HIV-1 fusion cofactor (or CCR5) expression in said contacted T cell is lower than the level of the HIV-1 fusion cofactor (or CCR5) expression in a T cell not contacted with said bead, as required by Applicants' claimed method.

Because Levine *et al.* (*Int. Immunol.*) do not either explicitly or inherently teach ***each and every limitation*** of Applicants' claimed invention, this reference cannot anticipate Applicants' claimed invention. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

VII. Rejection under 35 U.S.C. § 102(e) based on June *et al.*

Claims 1, 55, 87-90 and 92-94 stand rejected under 35 U.S.C. § 102(e) as being anticipated by June *et al.* (U.S. Patent No. 6,352,694) as evidenced by Levine *et al.* (*Science* **272**:1939-1942, 1996) (Office Action, page 7, section 14).

Claims 1, 55, 60, 75, 87-88 and 91-94 have been cancelled. Thus, this rejection as it applies to these claims has been rendered moot. However, we address this rejection as it may apply to the new claims 95-107.

Like Chang and Levine, described *supra,* June *et al.* also do not in any way teach or suggest measuring the level of HIV-1 fusion cofactor (or CCR5) expression in a T cell contacted with a bead comprising an anti-CD28 antibody or a fragment thereof and an anti-CD3 antibody or a fragment thereof, wherein the level of HIV-1 fusion cofactor (or CCR5) expression in said contacted T cell is lower than the level of the HIV-1 fusion cofactor (or CCR5) expression in a T cell not contacted with said bead, as required by Applicants' claimed method.

Because June *et al.* (*Int. Immunol.*) do not either explicitly or inherently teach ***each and every limitation*** of Applicants' claimed invention, this reference cannot anticipate Applicants' claimed invention. Thus, Applicants aver that the grounds for this rejection have been overcome. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

VIII. Rejection under 35 U.S.C. § 103 (June *et al.* in view of Chang)

Claims 60, 75 and 87-90 and 92-94 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over June *et al.* (U.S. Patent No. 6,352,694) as evidenced by Levine *et al.* (*Science* **272**:1939-1942,1996) in view of Chang (U.S. Patent No. 6,129,916) (Office Action, page 9, section 17).

Claims 60, 75, 87-90 and 92-94 have been cancelled. Thus, this rejection as it applies to these claims has been rendered moot. However, we address this rejection as it may apply to the new claims 95-107.

As discussed above, June *et al.* do not in any way teach or suggest measuring the level of HIV-1 fusion cofactor (or CCR5) expression in a T cell contacted with a bead comprising an anti-CD28 antibody or a fragment thereof and an anti-CD3 antibody or a fragment thereof, wherein the level of HIV-1 fusion cofactor (or CCR5) expression in said contacted T cell is lower than the level of the HIV-1 fusion cofactor (or CCR5) expression in a T cell not contacted with said bead, as required by Applicants' claimed method. This deficiency is not cured by either of the Levine or Chang references.

Accordingly, Applicants respectfully request that this rejection under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

IX. Rejection under the doctrine of obviousness-type double patenting

Claims 1, 55, 60, 75 and 87-94 stand rejected under the doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,352,694 either alone or in combination with Chang (U.S. Pat. No. 6,129,916) (Office Action, page 10, section 19).

Claims 1, 55, 60, 75, 87-88 and 91-94 have been cancelled. Thus, this rejection as it applies to these claims has been rendered moot. However, we address this rejection as it may apply to the new claims 95-107.

Newly added claims 95-107 are not obvious over claims 1-16 of U.S. Patent No. 6,352,694 either alone or in combination with Chang because the combination does not

teach or suggest Applicants' claimed method. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

X. Conclusion

Applicants aver that all of the outstanding rejections of record have been overcome by amendment and/or argument. Accordingly, the claims are now believed to be in condition for allowance. Applicants respectfully request that the Examiner issue a timely Notice of Allowance.

Applicants petition for a one-month extension of time to respond to the Office Action mailed November 5, 2003. Please debit our Deposit Account No. 08-0219 for the requisite fee. No additional fees are believed to be due in connection with this correspondence. However, if any fees are due, please charge any payments due or credit any overpayments to our Deposit Account No. 08-0219.

The Examiner is invited to telephone the undersigned at the telephone number given below in order to expedite the prosecution of the instant application.

Respectfully submitted,

Date: March 5, 2004

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